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Thyroid Function Screening & Dysfunction in Patients with Heart Failure: An Examination of Practice at the University of Kentucky Albert B. Chandler Hospital From 2007-2017

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Thyroid Function Screening & Dysfunction in Patients with Heart Failure: An Examination of Practice at the University of Kentucky Albert B. Chandler Hospital From 2007-2017

CAPSTONE PROJECT PAPER

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requirements for the degree of
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Abstract

Introduction: Heart failure constitutes a global pandemic affecting at least 26 million globally (an estimated 5.7 million of which are Americans), and its burden on our healthcare system is projected to increase.[1] As a result, it is imperative that diagnostics and treatment among that population be evidence based in order to contain costs and optimize patient outcomes. Over the last 20 years, thyroid function screening has been recommended for patients upon initial diagnosis of heart failure by the American College of Cardiology and other professional organizations. However, it remains unclear whether this recommendation is followed by practitioners and how much thyroid dysfunction screening uncovers. The aim of this capstone is to examine the association between thyroid dysfunction and heart failure and explore a practical example of thyroid function evaluation for patients newly-diagnosed with that disease.

Objectives: The primary objective of this study is to explore one medical center's hospitalizations associated with incident heart failure and determine how often and in which patients thyroid function is screened (using TSH). A secondary objective was to determine the amount of thyroid dysfunction discovered through that screening.

Methods: Participants in the current study were sampled from inpatient electronic medical records for patients at the University of Kentucky Albert B. Chandler Hospital from 2007-2017. Only first hospitalizations during which heart failure was documented were included in the study (N = 15900). Logistic regression was used to analyze the association between patient characteristics and the probability of receiving thyroid function screening during that hospital stay. Similar analysis was done to explore the association between patient characteristics and thyroid dysfunction among those screened.

Results: A minority (36.09%) of our patient population had their TSH tested during initial heart failure admission. In multivariable analysis, longer length of stay (OR: 1.33-2.18), year of encounter (OR: 1.03, 95% CI: 1.02-1.04), and female sex (OR: 1.29, 95% CI: 1.21-1.38) were significantly associated with increased odds of patients having their TSH tested. Among those tested, multivariate analysis revealed that female sex (OR: 1.34, 95% CI: 1.19-2.07) and longer length of stay (OR: 1.20 for 8-14 days; OR: 1.45 for 22+ days) were associated with increased odds of thyroid dysfunction (abnormal TSH). African American race [vs white], on the other hand, was associated with decreased odds of thyroid dysfunction (OR: 0.74, 95% CI: 0.59-0.93). Age 65+ was also associated with decreased odds of dysfunction (OR: 0.82, 95% CI: 0.67-0.998). Of all patients tested, 28% had thyroid dysfunction. The most common abnormality detected was high TSH with normal FT4 (11%).

Conclusion: This study suggested that, despite recommendations, only a minority of newly diagnosed heart failure patients who are hospitalized have their thyroid function screened. Furthermore, our data hint that thyroid function is not consistently tested on all heart failure patients but is tested more often in women and in patients with longer hospitalizations. Among those screened, thyroid dysfunction appeared to be more common than that reported in the general population but was still a minority of patients. The most common abnormality detected was subclinical hypothyroidism. We hope that knowing how often thyroid screening is performed, who specifically is screened, and what testing uncovers may

lead to more targeted, cost-effective screening in those who would derive the most benefit from that practice.

Introduction

This introduction outlines the study's objectives; provides background information on heart failure and thyroid dysfunction; offers current knowledge of the pathophysiology, the mechanisms, and the cardiovascular impact of the different stages of thyroid dysfunction in heart failure patients; and presents information on the recommendations for thyroid dysfunction screening.[2]

Study Objectives

The primary objective of this study is to explore one medical center's incident heart failure hospitalizations and determine how often and in which patients thyroid function is screened using Thyroid Stimulating Hormone (TSH). We hypothesize that a minority of patients will have their thyroid function checked during their initial heart failure hospitalization, that screening will not be uniform for the entire population (screening will be more common in patients with certain characteristics), and that thyroid function testing increases with time. A secondary objective was to determine the amount of thyroid dysfunction discovered through that screening. We hypothesize that dysfunction is more common in heart failure patients than in the general population.

Cardiovascular Disease and Heart Failure

1.1 A Brief Introduction to Cardiovascular Disease

Over the last decade, cardiovascular disease (CVD) has become the leading cause of death worldwide.[3] As more countries progress through the epidemiologic transition to the final stages to Degenerative/Man-Made and Delayed Degenerative Disease, the global burden of cardiovascular disease increases. Over 17 million deaths are attributable

to CVD each year—nearly a third of all deaths.[4] CVD also confers a heavy burden in terms of morbidity. CVD was responsible for over 365 million disability-adjusted life-years (DALYs) lost in 2017 alone.[4] These data represent increases in both absolute numbers and percentages of DALYs compared with 2015 estimates (355 million DALYs).[4]

1.2 Heart Failure: An Overview

Heart failure is a complex clinical syndrome characterized by impaired heart function (whether from filling or pumping). Risk factors for heart failure are varied and include myocarditis, valvular heart disease, tachycardia, diabetes mellitus, structural heart disease related to congenital heart disease, sleep apnea, excessive drug or alcohol use, obesity, and CVD (in particular, ischemic heart disease), which confers the highest risk of heart failure.[5, 6] Heart failure is a global pandemic affecting at least 26 million globally (an estimated 6.2 million of which are Americans).[1, 7] And the problem is growing—partly as a result of advances in treatment, demographic change (prevalence rises exponentially with age and affects 4% to 8% of people older than 65), and improved survival.[5] While incidence rates have reached a relative plateau, prevalence continues to rise.[8] In the US alone, it is estimated that heart failure prevalence will increase 46% from 2012- 2030.[9]

1.3 The Burden of Heart Failure

Unlike some non-communicable conditions that are largely managed in an outpatient setting (hyperlipidemia, for example), heart failure's burden is recurrent (characterized by a relapsing pattern), and the associated healthcare costs fall heavily on the hospital system.[10] In some areas of the United States, annual hospital readmission

rates are estimated to be as high as 50%.[11] In 2014 alone, 900,000 hospital discharges listed heart failure as the primary diagnosis.[7]

Thyroid Dysfunction

2.1 A Brief Introduction to Thyroid Function

The thyroid gland is an endocrine organ tasked with producing hormones that regulate a multitude of metabolic functions in the human body. Among others, thyroid hormones play a key role in growth, neuronal development, reproduction, and regulation of energy metabolism.[12] Consequently, defects in the formation of the thyroid, production of its hormones, or release of the same can contribute to a variety of adverse health effects. The thyroid gland secretes two primary hormones, T3 (3,5,3′-triiodothyronine—the more biologically active hormone) and T4 (3,5,3′,5′-tetraiodothyronine; also known as thyroxine).[13] These hormones mediate their multitude of effects via nuclear hormone receptors.

2.2 Thyroid Dysfunction: Basics

Thyroid dysfunction (a general term that encompasses both deficiency as well as overabundance of thyroid hormones) is common around the world and can have potentially devastating health consequences. While deficiency of iodine (an integral component of thyroid hormones) is reportedly the most common cause of thyroid disorders, dysfunction remains common in 'iodine sufficient' areas such as the United States.[14]

2.3 Thyroid Dysfunction: Diagnostic Definitions

Serum Thyroid Stimulating Hormone (TSH, also called serum thyrotropin), the major regulator of the thyroid, constitutes the single best indicator of its function.[15] While technically an indirect reflection of thyroid hormone supply (TSH is a stimulating hormone secreted by the pituitary), it is used as the initial and primary diagnostic instrument for several reasons. First, TSH is a central component of the negative-feedback system that regulates thyroid function. Second, TSH secretion is exquisitely sensitive to the plasma concentration of T3 & T4; small changes in serum thyroid function cause logarithmic amplification in TSH secretion.[16] Even minor fluctuations are detectable with advanced TSH assays, which are capable of discriminating values as small as <0.1mU.[16] TSH has a sensitivity of ~98% and specificity of ~92% when used to confirm clinically suspected thyroid disease by an endocrinologist.[17] However, its accuracy is difficult to ascertain when it is used to screen asymptomatic persons for thyroid dysfunction.

While TSH is often the initial thyroid function test used for screening, an abnormal value often prompts subsequent measurement of T4. Unfortunately, the determination of a TSH abnormality is not always straightforward. The normal range of serum TSH concentration varies slightly in different laboratories (sometimes defined this by a population range), but is now most commonly defined as 0.4 to 4.2 mU/L; This is the range of TSH prevalence levels in 96% of the disease- and risk-free population.[18] A complicating factor in the identification of thyroid dysfunction is the relative fluidity of

what is considered the 'normal range' over time. Over the last few decades, the upper limit of normal has gradually declined from 7.0-10 mU/L to 4.0–5 mU/L.[19]

Thyroid dysfunction can be further divided into that which is 'subclinical' versus 'overt'. Subclinical dysfunction can best be described as an early condition of mild thyroid hormone excess/deficiency in which thyroid hormones remain within the normal range. Subclinical hypothyroidism is characterized by a high serum TSH and a normal serum concentration of free T4 (measured as 'free' since the total level can be distorted by the level of carrier proteins to which thyroid hormones are bound); overt hypothyroidism has high TSH and a low free T4 serum concentration.[18] Subclinical hyperthyroidism, on the other hand, is defined by a low TSH and a normal free T4, and overt hyperthyroidism is described as a low TSH with a high free T4 serum concentration.[11] These definitions are reflected below in Reference Table 1. Most endocrinologists recommend repeat testing for those with lab values consistent with subclinical thyroid dysfunction within 2-3 months since borderline values may not reflect persistent dysfunction, though the clinical value of this practice is questionable.[19] Given the significance of TSH for screening, some researchers and clinicians specify levels of that hormone to further define subclinical dysfunction.[18]

One special combination of abnormal thyroid tests is worth mentioning: nonthyroidal illness syndrome (also known as euthyroid sick syndrome) is a condition encountered in patients with acute or chronic systemic illness. The laboratory parameters that define this syndrome are low T3, low/normal T4 and low/normal TSH.

This condition may affect 60 to 70% of critically ill patients, and values generally normalize if the illness resolves (thus hinting at a non-thyroidal etiology).[20]

Reference Table 1: Characterization of Thyroid Dysfunction: Typical Thyroid Function Tests

Disorder	TSH	Free T4
Overt Hyperthyroidism	↓	↑
Subacute Hyperthyroidism	↓	Normal
Overt Hypothyroidism	↑	↓
Subacute Hypothyroidism	↑	Normal

2.4 Thyroid Dysfunction: Incidence & Prevalence

The global prevalence and incidence of thyroid dysfunction are difficult to determine given differences in screening, diagnostic thresholds, assay sensitivities, iodine nutrition, etc.[12] In general, the overall prevalence of hyperthyroidism and hypothyroidism ranges from 0.5–4% in iodine-replete communities, and is 5–10 times higher in women than in men.[21] In the United States, approximately 0.3% suffer from overt hypothyroidism, but 4.3% have mild or subclinical hypothyroidism.[22] Hyperthyroidism has a prevalence of 1% to 2% in women and 0.1% to 0.2% in men.[23]

Most of the studies that have explored the epidemiology of thyroid dysfunction do not distinguish between primary thyroid dysfunction and that which is caused by other factors. TSH can be depressed, for example, in patients with psychiatric illness, non-thyroidal illness syndrome, pregnancy, hypothalamic-pituitary disorders, and among those taking certain medications (glucocorticoids, dopamine, somatostatin analogues,

amphetamines, dobutamine, bexarotene, bromocriptine).[24] Robust statistics for primary thyroid dysfunction in the population are unknown.

2.5 Thyroid Dysfunction Screening

The rationale behind thyroid function testing in asymptomatic individuals is early detection and treatment with the hopes of preventing complications arising from thyroid imbalance. Specifically, there is hope that screening may prevent morbidity and mortality from fractures, cancer, or cardiovascular disease. However, widespread screening and subsequent treatment of thyroid dysfunction can also result in harms due to labeling, false-positive results, overdiagnosis and overtreatment.

Appropriate use of thyroid function screening has been much debated, and current recommendations are inconsistent across both countries and medical specialties. Recently, the United States Preventive Services Task Force (USPSTF) concluded that, for nonpregnant, asymptomatic adults, "current evidence is insufficient to assess the balance of benefits and harms of screening for thyroid dysfunction in nonpregnant, asymptomatic adults."[25] The American Academy of Family Physicians has endorsed the USPSTF recommendation, but The American Thyroid Association recommends screening at age 35 years and every 5 years thereafter.[25, 26] The American Association of Clinical Endocrinologists recommends routine TSH measurement in older patients—age not specified—especially women.[27] Until the guidelines recently became 'inactive', the American College of Physicians recommended screening in women older than age 50 years with one or more symptoms possibly caused by thyroid disease.[27]

Although exact estimates of rates in the United States are unknown, screening for thyroid dysfunction by primary care providers seems to be a common practice in the developed world.[25] In the United Kingdom, for instance, an estimated 18-25% of adults receive thyroid function assessed annually.[28]

2.6 Conclusion

Needless to say, the high prevalence of both thyroid dysfunction and heart failure highlight a need for preventive & therapeutic strategies to reduce morbidity, mortality, and cost from both of these conditions. The development of such strategies hinges on a better understanding both of the mechanisms and of the long-term consequences of one on the other.

Literature Review

This literature review was conducted using Google Scholar and PubMed. The main key words employed in the literature review were: heart failure, heart failure diagnosis & management, cardiovascular disease, cardiovascular system, thyroid dysfunction, thyroid disease, subclinical thyroid dysfunction, thyroid screening, thyroid hormones, thyroid-stimulating hormone, hypothyroidism, and hyperthyroidism.

3.1 Historical Investigation of Thyroid Function & Cardiovascular Health

The first documented association between thyroid dysfunction and cardiovascular health dates back to 1878, when William Greenfield characterized a case of severe hypothyroidism occurring with vascular disease.[29] Following the development of radioimmunoassays to estimate TSH in 1965, more quantitative research could be

conducted. In 1976 Belgian researchers reported higher rates of coronary artery disease, left ventricular hypertrophy and left ventricular dilation in hypothyroid subjects compared with a euthyroid group.[13] But over the years, such associations were not found consistently.[30] And, when a trial of dextrothyroxine (lower activity isomer of T4) in male survivors of acute myocardial infarction demonstrated higher mortality and increased arrhythmias, clinicians became wary of the cardiovascular consequences of hyperthyroidism.[31] Over the past few decades, more detailed studies have demonstrated that even subtle changes in thyroid hormone concentrations (e.g. those observed in subclinical hypo or hyperthyroidism) can adversely affect the cardiovascular system.[13]

3.2 Thyroid Hormones & Cardiovascular Physiology

Many patients with thyroid dysfunction experience some type of cardiovascular manifestation, and it is believed that the most serious complications of thyroid disease occur as a result of cardiac involvement.[32] If left untreated, both overtly hypo- and hyperthyroidism accelerate the onset of symptomatic cardiovascular disease.[13] Thyroid hormone receptors are present throughout the body, including the myocardium and vascular tissue, which allow for hormone alterations to affect cardiovascular physiology such as chronotropy and inotropy.[13] Some mechanisms behind thyroid hormone's cardiovascular effects include endothelial dysfunction, dyslipidemia, changes in blood pressure, and myocardial systolic and diastolic dysfunction.[13]

3.3 Thyroid Dysfunction & Cardiovascular Health

In hyperthyroid patients, chronotropic effects of thyroid hormones manifest as tachycardia and increased risk of atrial fibrillation.[33] Other effects of excess thyroid hormones include increased cardiac output, myocyte hypertrophy, increased left ventricular mass, arterial stiffness and left atrial size.[24] Components that may contribute to heart failure include chronotropy, inotropy, and arrhythmogenic activity of the pulmonary veins.[11]

In contrast, hypothyroid patients demonstrate bradycardia and reduced cardiac contractility.[33] Hypothyroidism is also associated with reduced cardiac output, heart rate, and contractility along with increases in peripheral vascular resistance, diastolic blood pressure, cholesterol levels, and carotid intima-media thickness.[34] Several of these factors are likely instrumental in accelerating atherosclerosis.[13] Changes in coagulation parameters observed in hypothyroidism may also contribute to subsequent cardiovascular disease.[13] The most frequent cardiac abnormality seen with echocardiogram in individuals with hypothyroidism is diastolic dysfunction owing to impaired ventricular filling and relaxation.[13]

3.4 Subclinical Thyroid Dysfunction & Cardiovascular Health

Evidence regarding the association between subclinical thyroid dysfunction and cardiovascular outcomes is conflicting.[13] Some studies document positive associations with sudden cardiac death[35] and cardiovascular outcomes such as CVD morbidity & mortality.[11, 13, 24] One study found an increase in cardiovascular disease and death in hypothyroid patients but not hyperthyroid patients.[21] Others identify an increase in

mortality in hypothyroidism, but no corresponding increase in cardiovascular events.[35] To summarize, a multitude of studies have addressed this topic; while many lean towards the conclusion that subclinical thyroid disease may be associated with cardiovascular morbidity, no cause and effect can be proven in the absence of mechanistic studies and randomized clinical trials.[35]

3.5 Thyroid Dysfunction in Heart Failure

According to observational studies, subclinical hypothyroidism and nonthyroidal illness syndrome are the most frequent thyroid hormone alterations in patients with heart failure.[36] The latter is particularly common and occurs in an estimated 20-30% of patients with heart failure.[37] Unfortunately, both subclinical hypothyroidism and nonthyroidal illness syndrome (also called low T3 syndrome) have been associated with a poor prognosis.[13]

3.6 Thyroid Screening in Heart Failure Patients

Since the physiological effects of thyroid dysfunction on the cardiovascular system compromise cardiac function, and since we know thyroid disease may contribute to heart failure and can be associated with poor prognosis, thyroid function screening was considered by some to be a standard of care for new onset heart failure until recently.[11] The American College of Cardiology, jointly with the American Heart Association, first published guidelines for the evaluation and management of HF in 1995. In these initial recommendations, TSH was recommended for patients with atrial fibrillation or sinus rhythm with unexplained heart failure (class I and class II recommendations, respectively).[38] Subsequent guidelines published in 2001, 2005,

2009, and 2013 all recommended the measurement of thyroid function tests (especially TSH) in the initial laboratory evaluation of all patients presenting with heart failure (level of evidence: C).[39-42] The most recent guidelines published in 2017, however, do not mention thyroid testing.[43] Still, some highly utilized texts in cardiovascular medicine continue to recommend this practice.[5]

3.7 Conclusion

The field of cardiology is fortunate to have such an abundance of knowledge on standard risk factors and secondary preventive measures for both cardiovascular disease and heart failure. However, to address a disease with such a tremendous burden on population health, more research is needed to clarify the role of practices such as thyroid function screening. Knowing how often thyroid screening is performed, who specifically is screened, and what testing uncovers may lead to more targeted, cost-effective screening in those who would derive the most benefit from that practice—such knowledge can help distinguish whether thyroid function screening in this population constitutes a valuable tool that augments patient care or a misuse of healthcare resources.

Methods

4.1 Setting

The University of Kentucky Albert B. Chandler Hospital is a level 1 trauma, 569-bed acute care hospital located in Lexington, KY; it is part of the UK HealthCare enterprise. During the period of 2007-2017, this institution annually processed more than 30,000 individual inpatient discharges.[44]

4.2 Study Design & Sampling

This study used a clinical cohort to examine the practice of thyroid dysfunction screening in adults during their first known hospital admission that included a diagnosis of heart failure. Data for the current study were limited to the earliest inpatient hospital stay (also referred to as an inpatient encounter) during which heart failure was documented as a diagnosis from 2007 through 2017.

In December 2018, inpatient records among heart failure patients from 2004 to 2017 in Sunrise Clinical Manager, the electronic medical record used by the University of Kentucky inpatient services, were identified. University of Kentucky's Center for Clinical & Translational Science Biomedical Informatics Team extracted from their Enterprise Data Warehouse encounters including an ICD9 or ICD10 diagnosis of heart failure.* A diagnosis of heart failure during an encounter was identified using the following ICD-9 and ICD-10 code definitions documented at discharge: ICD-9 code of 428.x in any position and ICD-10 code of I50.x in any position. Information obtained included basic demographics and thyroid function tests. Using the encounter data, the first known inpatient stay associated with a documented diagnosis of heart failure was determined. Afterwards, first known heart failure admission encounters were narrowed to those taking place from 2007-2017. This was done for two reasons: first, electronic medical records were mandated at UK Healthcare in 2004 and it is possible that adjusting to this system makes early data less reliable; second, it allowed for three years of encounters that could help

* The project described was supported by the NIH National Center for Advancing Translational Sciences through grant number UL1TR001998. The content is solely the responsibility of the author and does not necessarily represent the official views of the NIH.

determine whether an admission from 2007 on was in fact the first heart failure hospitalization.[45]

4.3 Variables & Endpoints

All information was obtained from structured data elements and included: age at the time of encounter, gender, race, ethnicity, and BMI. Additional information included admission date, discharge date, presence of previously diagnosed heart failure or thyroid disease, prescription for the most common thyroid medications (see separate appendix for full list) filled in the past year, and values for the first TSH, Free T3, and Free T4 obtained during the encounter. Previously diagnosed heart failure was defined as a recorded heart failure ICD-9 or ICD-10 diagnosis (defined above) documented prior to the encounter—this information included diagnosis codes from inpatient hospital stays as well as emergency room visits and the EMR used for UK Healthcare's outpatient encounters [Ambulatory Electronic Health Record (AEHR)]. In a similar manner, previously diagnosed thyroid disease was determined by previous documentation of ICD-9 (240-246) or ICD-10 codes (E00-E07).

BMI values were categorized according to the common definitions of underweight, normal weight, overweight, and obese. Patient age was grouped into the following categories: <45, 45-55, 55-64, 65+ years. These age cutoffs were chosen based on definitions used in the derivation of premature Coronary Artery Disease and Atherosclerotic Cardiovascular Disease (ASCVD).[46, 47] For patients with no race or ethnicity documented, a label of 'unknown' was assigned.

Two outcomes of interest, thyroid function tested and thyroid dysfunction (among those tested), were used in separate analyses. To assess correlates of thyroid function testing, dichotomous variables were created to indicate whether or not patients had TSH performed during the supposed first observed heart failure admission. TSH was used both because it is the primary recommendation for initial screening and because every patient whose thyroid function was tested had their TSH evaluated. Normal ranges for thyroid function tests were chosen based on those used by the UK Healthcare chemistry laboratory, which reads the tests in question; They are included in Reference Table 2.

Reference Table 2: Normal Range (Age-based) for Thyroid Function Tests Used in This Study[48]

Thyroid Function Test Age range (years)	Normal Range
TSH 18-20yo 21+	 0.5-4.3 µIU/mL 0.4-4.2 µIU/mL
Free T4 17+	 0.8-1.7 ng/dL
Free T3 All ages	 2.2-4.0 pg/mL

4.4 Data Cleaning

Once the data were obtained, encounters without a documented date were eliminated. In order to restrict the data to inpatient admissions, encounters were limited to encounters lasting a duration of 1 day or more. Redundant entries were pared down; any encounters with an identical deidentified encounter ID were merged such that thyroid function studies were included. When more than one value for a thyroid function study was available for the initial value, the maximum was used. Encounters were

eliminated if they did not include a documentation of heart failure during the encounter. For each deidentified (unique) medical record number, the earliest of these remaining encounters was selected as the initial heart failure admission. Subsequently, encounters were eliminated if the patient had a previously documented diagnosis of heart failure or thyroid disease. Finally, encounters for patients under 18 years old at the time of encounter were removed.

4.5 Analysis

Overall, a cross-sectional analytic approach was used on the clinical cohort described. Descriptive statistics were conducted for all encounters and were compared for both TSH tested vs not and thyroid dysfunction among those tested vs not. Figures were created to visualize both the proportion of TSH testing per year as well as specific thyroid function tests ordered for all heart failure encounters.

Logistic regression analyses were performed to determine correlates of the independent variables listed above and whether TSH was tested (dependent variable). Thus, odds ratios for the known characteristics were reported. Bivariate analysis of each individual variable of interest was conducted first. Whether these variables reached significance determined which were included in the complete model. Finally, the model was refined with backwards elimination to establish variables in the final model. In this way, race, ethnicity, and age were eliminated from the model. Sex, year of encounter, and length of stay were retained for the final model. Models were run with BMI, age, and length of stay as both categorical (ordinal) and continuous variables. All three had

higher significance levels when modeled as continuous rather than categorical variables. Because of this, they were treated as continuous in the final model.

An identical strategy was used to explore any associations between the characteristics measured and thyroid dysfunction (defined by abnormal TSH). The dependent variable was dichotomized as TSH normal (within the normal range) vs abnormal. Logistic regression was used to estimate odds ratios for thyroid dysfunction among those tested for each characteristic measured. Whether these variables reached significance determined which were included in the complete model. This model was refined with backwards elimination to establish variables in the final model. The final dependent variables in the final model were: sex, length of stay, age 65 years +, and black/African American race (vs white).

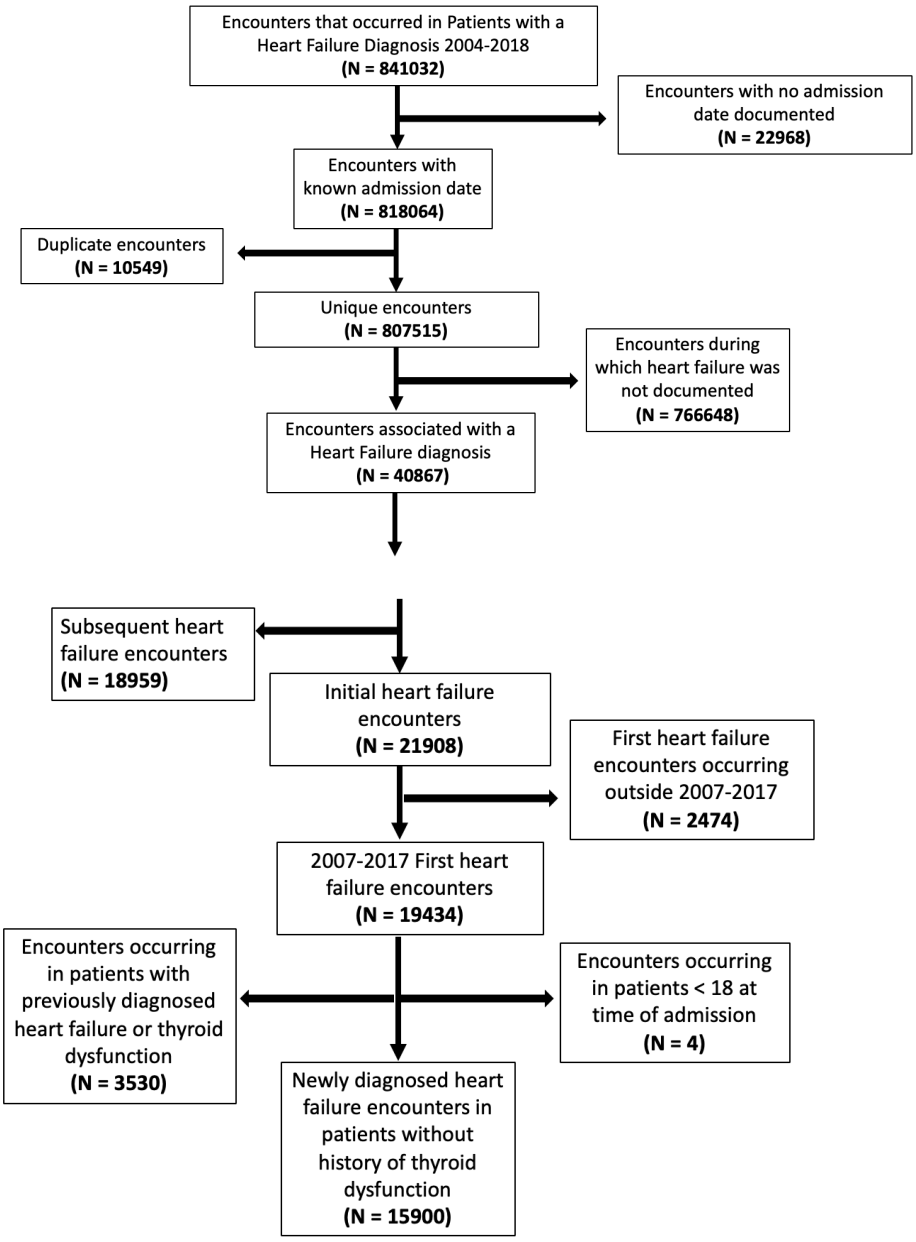
All analyses were conducted using SAS software, version 9.4 (SAS Institute; Cary, NC, USA).

Results

5.1 Final Data Set

Data for 841032 inpatient encounters were collected from 22491 unique patients who had heart failure documented at some point between 2004-2018. Exclusion criteria were applied to obtain a final data set consisting of 15900 encounters from unique patients occurring 2007-2017. These encounters met the criteria of initial heart failure encounters in adults with no known thyroid dysfunction. See Figure 1 for more details on specific exclusions.

Figure 1. Final Data Set Selection Process



5.2 Overall Encounter Characteristics

Tables 1 summarizes patient demographics in all patients encountered. The patients were 55% male and 45% female and mean age was 64.8 years (range 18-104). The number of participants was highest in the age group 65+ (52.74%), and lowest in the group <45 (9.26%). White participants dominated this study (constituting 89.58%); black/African American was second most prevalent race (7.43%), with very few others. Race was unreported or not provided for 2.3% of encounters. The majority (77.75%) of patients were non-Hispanic/Latino and 21.52% were unknown. Only 0.73% were Hispanic/Latino. Average BMI was 37.42kg/m^2, with the highest percentage of patients having a BMI over 30 kg/m^2 (41.74%). Average length of stay was 11.17 days, but most patients were hospitalized for 1-7 days (56.92%). The proportion of encounters during which TSH was tested increased over the study period from 6.18% in 2007 to 13.42% in 2017. Prevalence of thyroid screening in our population is presented in Figure 2. Over the study period, 36.09% of newly diagnosed heart failure patients had their TSH checked during hospitalization. Further information regarding of specific tests ordered during the inpatient encounters is presented in Figure 3.

5.3 Thyroid Function Screening

Table 2 reports demographics in patients with thyroid function tested vs not. Table 2 also includes results from bivariate logistic regression analysis, including unadjusted odds ratios, 95% confidence intervals and p-values to provide associations among covariates to thyroid function being tested. Thyroid function testing was significantly associated with female sex (p=<.01), length of stay (p=<.01) and year of

encounter (p=<.01). Race, ethnicity, and age were not significantly associated with thyroid function testing. Table 4 presents the results from multivariable logistic regression model for thyroid function testing. Adjusting for other covariates in the model, female sex, length of stay, and year of encounter remained significant (all p=<.01) in association with thyroid testing. Female patients had 1.29 times the odds of having their TSH tested in comparison to males. With each progressive year, the odds of TSH testing in this population increased by 0.03. Finally, the odds of testing increased with each subsequent length of stay interval.

5.4 Thyroid Dysfunction

Additionally, results are presented for the analysis of tested patients and whether they had thyroid dysfunction. Table 3 compares and contrasts demographics between tested patients who were found to have dysfunction vs not. Results of bivariate logistic regression are also included. Patients who underwent TSH testing were mostly white (89.00%) non-Hispanic/Latino (77.59%), slightly more male (51.19%) with a mean age of 65.08 years. There were no biracial subjects in this group. Mean BMI was 36.13 kg/m^2 and mean length of stay was 13.71 days. Bivariate analysis using the created variable 'dysfunction' suggested that female sex, African American/black and unreported race, and length of stay 8-14 or 22+ days were associated with increased thyroid dysfunction (p=<.01, .01, .04, .01, <.01 respectively). Age 65+ was associated with decreased odds of dysfunction (p=.0459). Year of encounter, BMI, other races, & ethnicity did not show a significant association with thyroid dysfunction.

Table 5 presents results from multivariate logistic regression model for thyroid dysfunction, including the variables of female sex, length of stay (8-14 & 22+ days), black/African American race, unreported/refused race, and age. Adjusting for other covariates, patients who were female (OR 1.34, p=<.01), or whose hospital stay lasted 8-14 days or 22+ days (OR 1.2 and 1.45 respectively) had increased odds of thyroid dysfunction. The designation of unreported/refused for race lost its significance. In analysis adjusted for sex and length of stay, Black/African American patients, had 0.74 (p=0.01) times the odds of thyroid dysfunction when compared to whites among patients with an incident heart failure hospitalization. Age over 65 was associated with decreased risk of thyroid dysfunction (OR: 0.82, p=0.048).

Discussion

6.1 Introduction

To my knowledge, this is the first study to examine frequency of thyroid function testing in adult patients admitted to the hospital with heart failure, and the first to examine the characteristics of those tested vs not. The purpose of this study was to identify the frequency with which adults initially admitted for heart failure had their thyroid function checked at the University of Kentucky Albert Chandler hospital over the period 2007-2017 and to describe the frequency of thyroid dysfunction observed in those patients.

6.2 Frequency of Thyroid Function Screening

Despite the recommendations to screen for thyroid dysfunction in this patient population, a minority of patients (36.09%) had their TSH tested in this study. Unfortunately, no studies have previously examined thyroid function screening in patients with heart failure. So, it is unclear how these results would compare to a broader population. It may be that many clinicians are carefully considering the lack of evidence behind this recommendation (level C) and have largely chosen not to universally screen initial heart failure patients. In conjunction with this, providers may be taking into account other patient risk factors for heart failure. In a patient with multiple comorbidities, they determine that likelihood heart failure is due to thyroid dysfunction is low. For patients that tend to receive most of their care within the UK Healthcare system, practitioners may deem screening unnecessary if they have been tested relatively recently.

Longer hospital stays were associated with increased odds of testing. (ORs: 1.33, 1.69, 2.18 for 2, 3, and more than 4 weeks respectively). It is reasonable to (on average) consider a longer length of stay indicative of a more severe illness. In such patients, it is often practical to ensure no easily treatable contributing factors like thyroid dysfunction can be addressed while the patient is in the hospital. A longer length of stay also allows for more opportunities for different providers to order thyroid function studies.

While the magnitude of the association is not particularly strong (OR: 1.03, 95% CI: 1.02-1.04), there was a significant increase in testing frequency with each progressive

year. This may reflect greater availability of tests, increased ease of ordering, and/or better resources with regard to informing providers of ACC recommendations.

Controlling for length of stay and year, female patients had 1.29 times the odds of having their thyroid function screened versus males (95% CI: 1.21-1.38). We do know that females are more likely to suffer from thyroid dysfunction than their male counterparts, and this alone may account for more thyroid function testing among females.[30] In other words, providers that recognize gender as a risk factor may consider testing to be of higher value in this population. However, it is also true that women are underdiagnosed and undertreated with regard to cardiovascular disease, and are less likely to receive preventive treatment and guidance than are men at a similar ASCVD risk.[49-51] Because practitioners are less likely to recognize cardiovascular disease in women (strongest risk factor for heart failure), they may be searching for an alternate etiology.

6.3 Thyroid Dysfunction Among Screened Patients

Among the patients screened for thyroid dysfunction, most patients had a TSH (72%) within the normal range. In total, 28% of those tested revealed some sort of thyroid dysfunction. A study that included hospitalized patients aged 65 or older demonstrated 17.4% thyroid dysfunction.[52] Patients hospitalized with COPD exacerbation had 20% abnormal TSH.[53] In patient screened in the CORONA trial (which sought to examine the effect of low-dose rosuvastatin on survival in heart failure), 8.7% were discovered to have thyroid dysfunction using a broader normal range for TSH.[54] Thus, our study suggests thyroid dysfunction may be more prevalent among our group of

patients initially diagnosed with heart failure as compared with other hospitalized groups—even other groups diagnosed with heart failure.

The most common thyroid dysfunction among those tested was high TSH with normal FT4 (11%). This is concordant with many observational studies which have shown this pattern (consistent with subclinical hypothyroidism).[36] Nonthyroidal illness syndrome, another common thyroid hormone disturbance in ill patients, could not be adequately evaluated since the TSH values may be normal in this condition and T3 was rarely measured.

Among screened patients, multivariate analysis revealed that female sex (OR: 1.33, 95% CI: 1.18-1.49) was associated with increased odds of thyroid dysfunction (abnormal TSH). This is in agreement with studies that have consistently found prevalence of thyroid dysfunction is much higher in females than males in the general population.[55, 56]

To some extent, increasing length of stay was also associated with increased odds of thyroid dysfunction (8-14 days and 22+ days OR: 1.20 & 1.45 respectively). Interestingly, the 15-21 day range did not reach significance. While dysfunction increasing with time could be secondary to longstanding illness, disease severity was not ascertained in this study. Since any differential of greater comorbidity among longer hospitalization is unknown, this is highly speculative. It is unclear why the middle range did not reach significance.

African American race [vs white], was associated with decreased odds of thyroid dysfunction (OR: 0.74, 95% CI: 0.59-0.93). In a large prospective study in Brazil, Olmos, et

al. demonstrated that African Americans had less thyroid dysfunction overall, but that this was mainly a result of less overt hypothyroidism (OR = 0.76) despite increased overt hyperthyroidism (OR = 1.82).[57] While this study did not examine the particular types of thyroid dysfunction, it is concordant with this and other studies that conclude African Americans have a lower prevalence of thyroid dysfunction as a whole.[17, 58]

Age was included in the final model since it is consistently associated with thyroid dysfunction in the literature.[55, 59] Multiple studies have shown the incidence and prevalence of both hypo and hyperthyroidism increased with age.[60, 61] Hypothyroidism, for example, seems to climb with each decade—it ranged from 4 to 21% in women and 3 to 16% in men.[62] In our study, only the age range of 65+ showed an association with thyroid dysfunction—and this was a negative association. This is puzzling, as we would expect the opposite. It is possible that the selection bias inherent in studying a disease more common in the elderly has made age as a covariate less reliable.

While race 'unreported' [vs white] was initially associated with increased odds of thyroid dysfunction, this variable did not maintain significance in the final model (p=.06).

6.4 Limitations: population, characteristics/measurements, analysis

Thyroid function screening in newly diagnosed heart failure patients is an understudied aspect of heart failure management. Though this study is unique in its examination of this issue, it is not without limitations. Encounters were restricted to patients admitted to a single hospital within the UK Healthcare setting. The study therefore relied on a small sample of heart failure patients—and ones that are unique to

the University of Kentucky. It is only by considering encounters across the whole spectrum of acute and chronic care that the full picture of practice and prevalence can be captured. Heart failure may be both diagnosed and treated solely in an outpatient setting, and these cases are not accounted for in this analysis. In two studies, the proportion of heart failure diagnoses occurring in an outpatient setting ranged from 31 to 42%.[63] When emergency department visits are included (for patients diagnosed but not admitted), the proportion may be as high as 52%.[64] This study does not capture this 'outpatient' subset of heart failure patients.

Misclassification may have occurred since we have very limited data on patients, and a validated ascertainment protocol was not utilized. As a result, heart failure ascertainment, in particular, may have been very inaccurate. Since any diagnostic position was used to define a heart failure encounter, a substantial proportion of the primary reason for hospitalization may not have been heart failure-related. And, since this data only covers a single EMR, any outside medical care is unaccounted for. We may have, for instance, identified an encounter as an initial heart failure encounter when that individual simply has chronic heart failure but just recently started receiving care at UK.

There are innumerable potential confounding factors that this study was unable to account for. For example, it was not possible to obtain reliable data on which provider ordered the thyroid function tests. It is entirely possible that provider preference is the dominant determinant of thyroid function testing. And, while odds ratios suggest that differences in patient characteristics between tested and not-tested patients were small,

we did not have comprehensive data on comorbidities, family history, or vital signs (just to name a few).

It should be stressed that what constitutes an abnormal TSH level is uncertain. Laboratories use reference intervals based on statistical distribution across a population rather than based on clinical outcomes, and different TSH cutoffs are used to define subclinical thyroid dysfunction in particular.[25] This study has defined undifferentiated thyroid dysfunction using these parameters, and therefore cannot comment on its relation to increased risk of adverse outcomes, or on more specific types of thyroid dysfunction. TSH secretion does fluctuate during the day, with peak values in the early morning and a nadir in the afternoon.[18] As the more common lab draws obtained in the hospital do occur early in the morning, it is possible that the study has effectively over-diagnosed some patients. It is also unknown how many (if any) patients were tested based on symptoms rather than blanket screening.

6.5 Further Comments

Despite the published recommendation to obtain thyroid function tests (especially TSH) since 1995, this study demonstrated that at UK Albert Chandler Hospital, obtaining TSH is not very common among HF patients, though testing in this specific population may have slightly increased over the study period. While no formal explanation was offered, the failure to maintain this recommendation in a 2017 update may reflect doubt as to its cost-efficacy and value to patient care.

Proponents of screening claim that erring on the side of caution to detect a treatable condition is the prudent choice—particularly since overt thyroid dysfunction is

associated with adverse sequelae such as increased bone turnover, osteoporosis, and fractures.[24] Furthermore, studies have shown that in-hospital TSH values are highly concordant with ambulatory values in patients over 65 (our main heart failure population), and thus may not need to be repeated prior to initializing treatment.[52] While there is some evidence from prospective studies that even subclinical hypothyroidism and congestive heart failure are correlated, questions remain: which comes first, when do we treat, does screening improve patient outcomes, and is it cost effective.[65]

At this time, the benefit of thyroid function testing both in the general population and in heart failure patients is unknown. Furthermore, epidemiological evidence supporting treatment of subclinical dysfunction especially is limited and results are mixed.[25]

Not only are 'normal ranges' of TSH unknown, currently there is a lack of consensus on when treatment for thyroid dysfunction (subclinical especially) is indicated.[25] This is true of the general populace as well as those hospitalized with heart failure. So to a certain extent screening is of limited value. Finally, it is important to think of all possible consequences of screening. For example, a large magnitude of overdiagnosis and overtreatment likely follows from screening asymptomatic individuals. USPSTF aptly states that "overdiagnosis leads to psychological consequences and unnecessary treatment…it should be avoided in disease prevention and health promotion."[25]

6.6 Next Steps

More research is needed in this area. Specifically, studies need to evaluate harms and benefits of thyroid screening in heart failure patients in order to establish whether the practice confers a health benefit. Studies are also needed to explore what TSH values should serve as clinically meaningful cutoffs for diagnosis and treatment. Finally, we need to investigate long-term outcomes of thyroid dysfunction in heart failure patients.

6.7 Conclusions

Despite progress made in the management of heart failure, this syndrome is still associated with poor clinical outcomes including a high risk of mortality.[11] Its burden on the healthcare system is high—heart failure was responsible for an estimated 31 billion dollars of health care expenditure in 2012 (not counting indirect costs & loss of productivity).[1] Its costs are projected to increase by 46% by 2030. Nearly 80% of the projected expenses are attributable to increased hospitalizations.[10] In order to reduce hospitalizations and related costs, management strategies should be based on high-quality evidence. Gaining better understanding of all factors that contribute to heart failure can help formulate interventions aimed at decreasing incidence, prevalence, and the burden of heart failure on our healthcare system. In the same vein, it is important to recognize which steps can be taken to reduce costs during heart failure hospitalizations and avoid harms of interventions. Thyroid function screening is a practice that is commonly performed in heart failure patients despite lacking evidence on improved outcomes. More research is needed to determine how screening is used and what population it is most likely to benefit.

This study explored the use of thyroid function screening in newly diagnosed heart failure patients hospitalized at the University of Kentucky Albert B. Chandler Hospital from 2007-2017. The results suggest that, despite recommendations, only a minority of newly diagnosed heart failure patients who are hospitalized have their thyroid function screened. Furthermore, our data hint that thyroid function is not consistently tested on all heart failure patients but is tested more often in women and patients with longer hospitalizations. Screening also increased over time. Among those screened, thyroid dysfunction appeared to be more common than that reported in the general population but was still a minority of patients. The most common abnormality detected was subclinical hypothyroidism. We hope that knowing how often thyroid screening is performed, who specifically is screened, and what testing uncovers may lead to more targeted, cost-effective screening in those who would derive the most benefit from that practice.

Further studies should investigate the role of thyroid dysfunction across the natural history of cardiovascular disease in general (and heart failure specifically) to gain a better understanding of the underlying mechanisms. Not only are studies needed to clarify the benefits and harms of screening in this population, but randomized controlled trials should be conducted to demonstrate benefit of treatment and establish an evidence-based threshold for treatment.

Appendix

Table 1. Characteristics of Adult Patients During First Known Hospital Admission with Documentation of Heart Failure at the University of Kentucky Albert B. Chandler Hospital from 2007-2017

Characteristic	Mean value
Age (years)	64.80
BMI (Kg/m^2)	37.42*
Length of Stay (days)	11.17
Characteristic	**Encounters---N (%)**
TOTAL N (%)	15900 (100)
Sex	-
Male	8732 (55)
Female	7168 (45)
Race	-
White	14243 (89.58)
Black/African American	1181 (7.43)
Asian	40 (0.25)
Spanish American	38 (0.24)
American Indian/Alaskan	14 (0.09)
Middle Eastern	10 (0.06)
Hawaiian/Pacific Islander	6 (0.04)
Bi-racial	3 (0.02)
Unreported/Refused	365 (2.30)
Ethnicity	-
Non-Hispanic/Latino	12362 (77.75)
Hispanic/Latino	116 (0.73)
Unreported/Refused	3422 (21.52)

Characteristic	Encounters---N (%)
Age at admission	-
<45	1472 (9.26)
45-54	2202 (13.85)
55-64	3840 (24.15)
65+	8386 (52.74)
BMI (kg/m^2)	-
< 18.5	586 (3.69)
18.5–24.9	3579 (22.51)
25-29.9	3917 (24.64)
30+	6636 (41.74)
Unknown	1182 (7.43)
Length of stay (days)	-
1-7 days	9050 (56.92)
8-14 days	3391 (21.33)
15-21 days	1417 (8.91)
22+	2042 (12.84)
Year of encounter	-
2007	983 (6.18)
2008	914 (5.75)
2009	988 (6.21)
2010	1234 (7.76)
2011	1426 (8.97)
2012	1289 (8.11)
2013	1372 (8.63)
2014	1647 (10.36)
2015	1883 (11.84)
2016	2030 (12.77)
2017	2134 (13.42)

Table 2. Bivariate Analysis of Patient Encounter Characteristics and Thyroid Screening for Adult Patients During First Known Hospital Admission with Documentation of Heart Failure at the University of Kentucky Albert B. Chandler Hospital from 2007-2017

Characteristic TOTAL N=15900	Thyroid function not tested N=10162 (63.91%)	Thyroid function tested N=5738 (36.09%)	Crude Odds Ratio	95% CI	*p*- value
Sex	-	-	-	-	-
Male	5795 (57.03)	2937 (51.19)	Ref	Ref	Ref
Female	4367 (42.97)	2801 (48.81)	1.27	1.19,1.35	<.0001
Race	-	-	-	-	-
White	9136 (89.90)	5107 (89.00)	Ref	Ref	Ref
Black/African American	724 (7.12)	457 (7.96)	1.13	1.00,1.28	0.051
Asian	20 (0.20)	20 (0.35)	1.79	0.96,3.33	0.07
Spanish American	24 (0.24)	14 (0.24)	1.04	0.54,2.02	0.90
American Indian/Alaskan	9 (0.09)	5 (0.09)	0.99	0.33,2.97	0.99
Middle Eastern	9 (0.09)	1 (0.02)	0.20	0.03,1.57	0.13
Hawaiian/Pacific Islander	4 (0.04)	2 (0.03)	0.89	0.16,4.89	0.90
Bi-racial	3 (0.03)	0 (0.00)	*	*	*
Unreported/Refused	228 (2.24)	132 (2.30)	1.01	0.82,1.26	0.90
Ethnicity	-	-	-	-	-
Non-Hispanic/Latino	7910 (77.84)	4452 (77.59)	Ref	Ref	Ref
Hispanic/Latino	65 (0.64)	51 (0.89)	1.39	0.96,2.02	0.08
Unreported/Refused	2187 (21.52)	1235 (21.52)	1.00	0.93,1.09	0.93
Age at admission	-	-	-	-	-
<45	931 (9.16)	541 (9.43)	Ref	Ref	Ref
45-54	1452 (14.29)	750 (13.07)	0.80	0.77,1.02	0.09
55-64	2476 (24.37)	1364 (23.77)	0.95	0.84,1.07	0.40
65+	5303 (52.18)	3083 (53.73)	1.00	0.89,1.12	0.99
BMI	-	-	-	-	-
< 18.5	381 (3.75)	205 (3.57)	Ref	Ref	Ref
18.5–24.9	2282 (22.46)	1297 (22.60)	1.06	0.88,1.27	0.56
25-29.9	2481 (24.41)	1436 (25.03)	0.98	0.90,1.29	0.43
30+	4222 (41.55)	2414 (42.07)	1.06	0.89,1.27	0.50
Unknown	796 (7.83)	386 (6.73)	0.90	0.73,1.11	0.33
Length of stay (days)	-	-	-	-	-
1-7 days	6223 (61.24)	2827 (49.27)	Ref	Ref	Ref
8-14 days	2113 (20.79)	1278(22.27)	1.33	1.22,1.45	<.0001
15-21 days	801 (7.88)	616 (10.74)	1.69	1.51,1.90	<.0001
22+	1025 (10.09)	1017 (17.72)	2.18	1.98,2.41	<.0001
Year of encounter	-	-	-	-	-
2007	670 (6.59)	313 (5.45)	1.03	1.02,1.04	<.0001
2008	593 (5.84)	321 (5.59)			
2009	669 (6.58)	319 (5.56)			
2010	816 (8.03)	418 (7.28)			
2011	874 (8.60)	552 (9.62)			
2012	804 (7.91)	485 (8.45)			
2013	915 (9.00)	457 (7.96)			
2014	1118 (11.00)	529 (9.22)			

2015	1225 (12.05)	658 (11.47)			
2016	1222 (12.03)	808 (14.08)			
2017	1256 (12.36)	878 (15.30)			

*Numbers too small to estimate a stable OR

Table 3. Bivariate Analysis of Adult Patients Screened for Thyroid Dysfunction During First Known Hospital Admission with Documentation of Heart Failure at the University of Kentucky Albert B. Chandler Hospital from 2007-2017

Characteristic TOTAL N=5738	No Thyroid Dysfunction N=4133 (72.03%)	Thyroid Dysfunction N= 1605 (27.97%)	Crude Odds Ratio	95% CI	*p*- value
Sex	-	-	-	-	-
Male	2197 (53.16)	740 (46.11)	Ref	Ref	Ref
Female	1936 (46.84)	865 (53.89)	1.33	1.18,1.49	<.0001
Race	-	-	-	-	-
White	3662 (88.60)	1445 (90.03)	Ref	Ref	Ref
Black/African American	354 (8.57)	103 (6.42)	0.74	0.59,0.93	0.01
Asian	18 (0.44)	2 (0.12)	0.28	0.07,1.22	0.09
Spanish American	9 (0.22)	5 (0.31)	1.41	0.47,4.21	0.54
American Indian/Alaskan	5 (0.21)	0 (0)	*	*	*
Middle Eastern	0 (0)	1 (0.06)	*	*	*
Hawaiian/Pacific Islander	1 (0.02)	1 (0.06)	2.53	0.16,40.54	0.51
Bi-racial	0 (0)	0 (0)	*	*	*
Unreported/Refused	84 (2.03)	48 (2.99)	1.45	1.01,2.08	0.04
Ethnicity	-	-	-	-	-
Non-Hispanic/Latino	3230 (78.15)	1222 (76.14)	Ref	Ref	Ref
Hispanic/Latino	40 (0.97)	11 (0.69)	0.73	0.37,1.42	0.35
Unreported/Refused	863 (20.88)	372 (23.18)	1.14	1.00,1.31	0.06
Age at admission	-	-	-	-	-
<45	371 (8.98)	170 (10.59)	Ref	Ref	Ref
45-54	544 (13.16)	206 (12.83)	0.83	0.65,1.05	0.12
55-64	977 (23.64)	387 (24.11)	0.86	0.70,1.07	0.19
65+	2241 (54.22)	842 (52.46)	0.82	0.67,1.00	0.0495
BMI	-	-	-	-	-
< 18.5	140 (3.39)	65 (4.05)	Ref	Ref	Ref
18.5–24.9	934 (22.60)	363 (22.60)	0.81	0.59,1.13	0.22
25-29.9	1052 (25.45)	384 (23.93)	0.77	0.55,1.06	0.11
30+	1745 (42.22)	669 (41.68)	0.81	0.59,1.10	0.18
Unknown	262 (6.34)	124 (7.73)	0.97	0.67,1.41	0.88
Length of stay (days)	-	-	-	-	-
1-7 days	2110 (51.05)	717 (44.67)	Ref	Ref	Ref
8-14 days	905 (21.90)	373 (23.24)	1.21	1.05,1.41	0.01
15-21 days	439 (10.62)	177 (11.03)	1.187	0.98,1.44	0..08
22+	679 (16.43)	338 (21.06)	1.47	1.25,1.71	<.0001
Year of encounter	-	-	-	-	-
2007	221 (5.35	92 (5.73)	1.01	0.992,1.030	0.25
2008	237 (5.73)	84 (5.23)			
2009	220 (5.32)	99 (6.17)			
2010	323 (7.82)	95 (5.92)			
2011	413 (9.99)	139 (8.66)			
2012	350 (8.47)	135 (8.41)			
2013	331 (8.01)	126 (7.85)			
2014	368 (8.90)	161 (10.03)			
2015	469 (11.35)	189 (11.78)			
2016	567 (13.72)	241 (15.02)			
2017	634 (15.34)	244 (15.20)			

*Numbers too small to estimate stable OR

Table 4. Logistic Regression of Patient Characteristics for Thyroid Function Screening Among Adult Patients During First Known Hospital Admission with Documentation of Heart Failure at the University of Kentucky Albert B. Chandler Hospital from 2007-2017

Characteristic	Adjusted OR	95% CI	*p*-value
Sex	-	-	-
Male	Ref	Ref	Ref
Female	1.29	1.22,1.39	<.0001
Year of Encounter	1.03	1.02,1.04	<.0001
Length of Stay (days)	-	-	-
1-7 days	Ref	Ref	Ref
8-14 days	1.32	1.22,1.44	<.0001
15-21 days	1.69	1.51,1.89	<.0001
22+	2.21	2.01,2.44	<.0001

Table 5. Logistic Regression of Patient Characteristics for Thyroid Dysfunction Among Adult Patients Screened for Thyroid Dysfunction During First Known Hospital Admission with Documentation of Heart Failure at the University of Kentucky Albert B. Chandler Hospital from 2007-2017

Characteristic	Adjusted OR	95% CI	*p*-value
Sex	-	-	-
Male	Ref	Ref	Ref
Female	1.35	1.20,1.51	<.0001
Length of Stay (days)	-	-	-
1-7 days	Ref	Ref	Ref
8-14 days	1.20	1.03,1.39	0.02
15-21 days	1.18	0.97,1.43	0.10
22+	1.45	1.23,1.70	<.0001
Race	-	-	-
White	Ref	Ref	Ref
Black/African American	0.74	0.59,0.93	0.01
Unreported/Refused	1.41	0.98,2.02	0.06
Age at admission	-	-	-
<45	Ref	Ref	Ref
45-54	0.86	0.67,1.09	0.21
55-64	0.88	0.70,1.09	0.24
65+	0.82	0.67,0.998	0.048

Figure 2. Thyroid Function Testing Over Time for Adult Patients During First Known Hospital Admission with Documentation of Heart Failure at the University of Kentucky Albert B. Chandler Hospital from 2007-2017

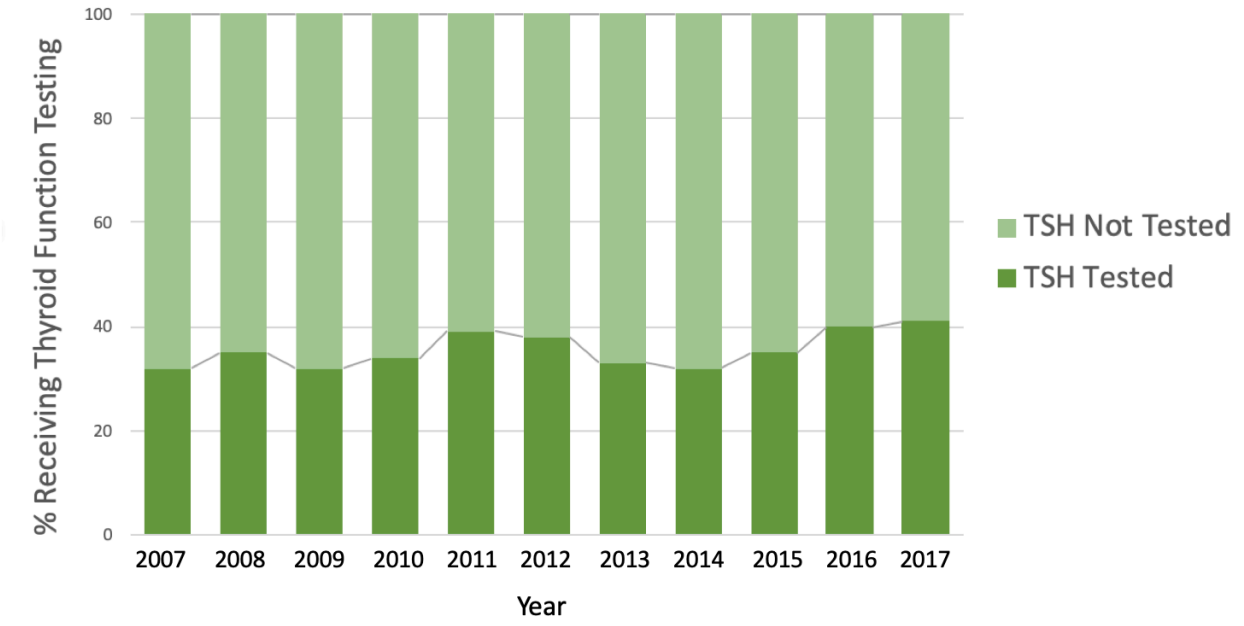


Figure 3. Specific Thyroid Function Studies Performed on Adult Patients Screened for Thyroid Dysfunction During First Known Hospital Admission with Documentation of Heart Failure at the University of Kentucky Albert B. Chandler Hospital from 2007-2017

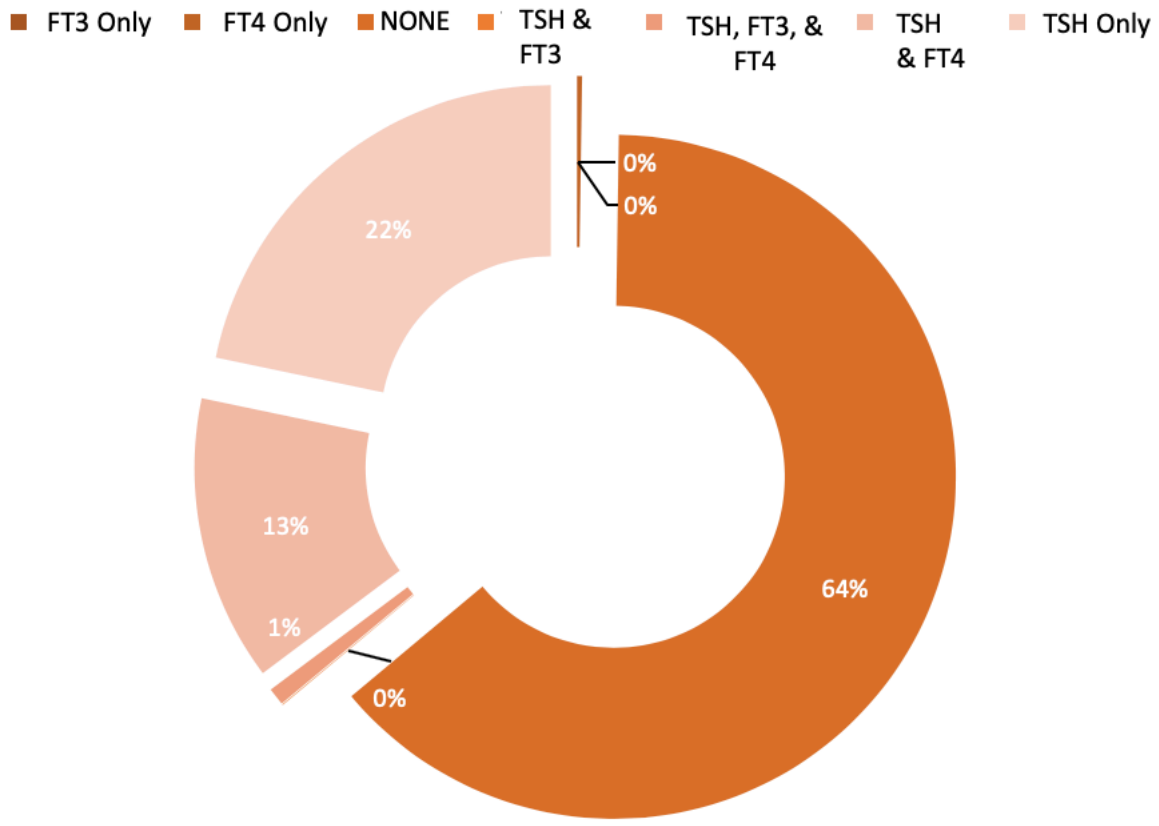


Figure 4. Thyroid Dysfunction Detected Among Those Patients Screened for Thyroid Dysfunction During First Known Hospital Admission with Documentation of Heart Failure at the University of Kentucky Albert B. Chandler Hospital from 2007-2017

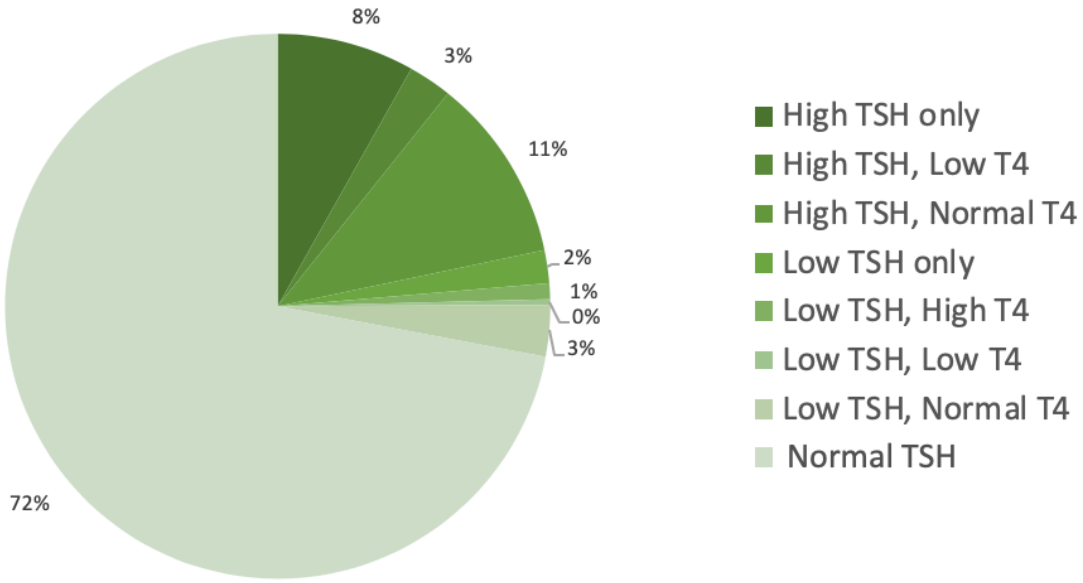
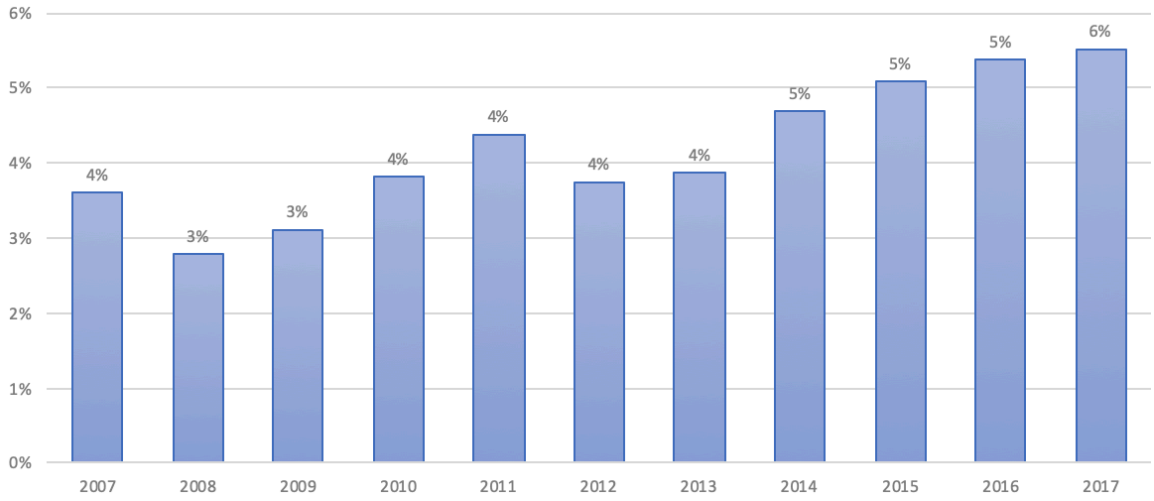


Figure 5. Hospitalizations Associated with Heart Failure as a Percentage of Total Discharges at the University of Kentucky Albert B. Chandler Hospital from 2007-2017



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